

Develop and test drugs with microjoint chip

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Motivation

- In the US, there are > 30 million patients with osteoarthritis (OA), with an economic burden at \$136.8 billion/year.
- OA causes pain, stiffness, reduced mobility, disability.....
- There is NO FDA-approved drugs to cure OA.
- Pain killers eventually lose efficacy.
- Final solution: total joint replacement.
 - A major surgery with complications.
 - Not recommended to 4 million young patients
- Insufficiency of Current Models in Developing OA Drugs

Project Description

We will create three-dimensional (3D), multi-component, human cell-derived, microphysiological knee joint-on-a-chip (microJoint) for drug development.

Context

- Current in vitro models do not fully encompass the “whole joint disease” nature of OA; alternatively, animal models have inherent deficiencies because of anatomical/physiological/genomic differences with humans.
- The tissue chip developed here will be included multiple human cells-derived joint tissues and connect them in a physiological manner (Chart 1).

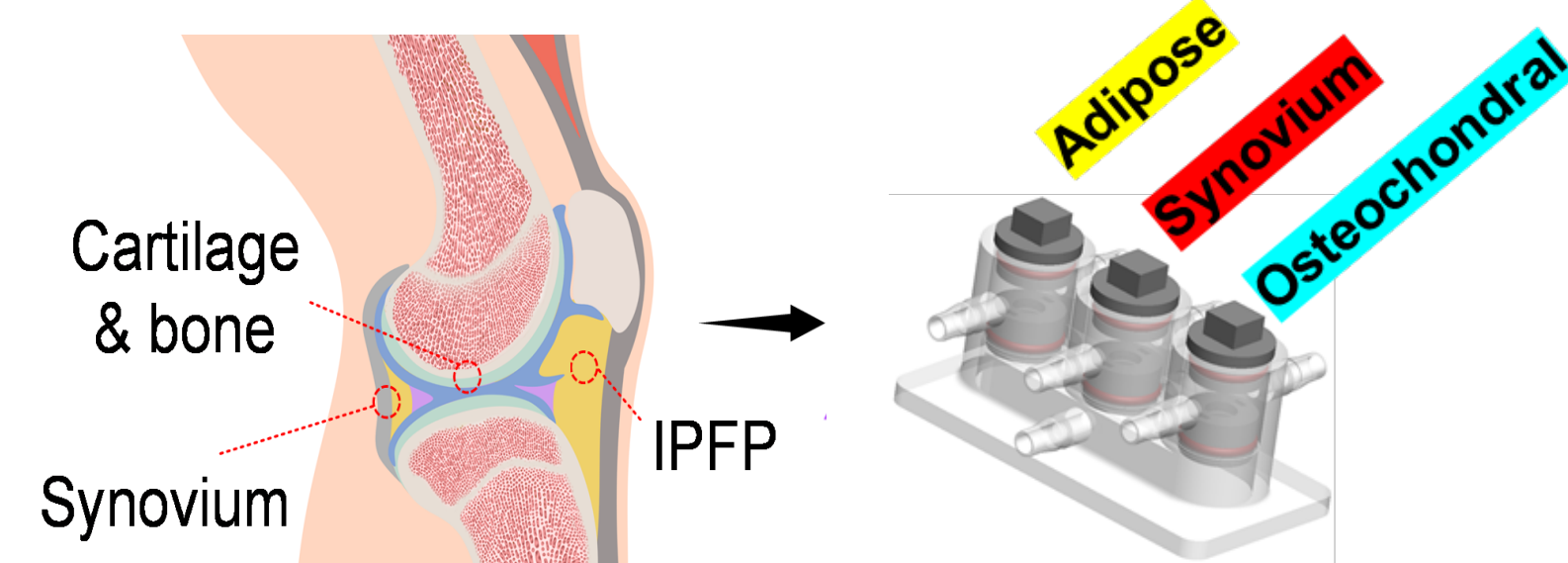


Chart 1. The microJoint – a microphysiological system mimicking the knee joint in the human body.



Primary project goal is to increase our power in **predicting** drug efficacy and toxicity, thus **reducing** the use of **animals** and **costs** for drug development.



Project Deliverables

- (1) Introduction of our team to Dr. Hochberg (M 1-2)
- (2) Preparation of the iPSCs and materials for new MPS-joint (M 1-2).
- (3) Fabrication of MPS-joint platform with PDMS (without the mechanism of applying mechanical force (M2-3).
- (4) Preparation of micro-particles for controlled release (M 1-2)
- (5) Examination of the drug loading capacity of micro-particles (M 2-3)
- (6) Creation of new MPS-joint in the PDMS platform (M 4-5)
- (7) Fabrication and assessment of mechanics-enabled MPS-joint (M 4-8)
- (8) Attending the Military Health System Research Symposium (MHSRS) 2021 meeting (M 8)
- (9) Creation of OA model in mechanics-enabled MPS-joint via mechanical overloading (M 8-9)
- (10) Examination of release profile of drugs from micro-particles (M 6-9)
- (11) Inviting Dr. Hochberg to the University of Pittsburgh (M 9)
- (12) Generation of OA mechanics-enabled MPS-joint for drug testing (M 10-12)

Potential Impact

Current in vitro cell culture and laboratory animal models may not be able to fully identify the unexpected poor treatment outcomes in humans. In our recently developed microJoint tissue chip, the novel multi-flow design (Chart 1) allows the introduction of treatments directly to the “synovial fluid”, or through other tissues from another medium stream. Through the use of patient-derived cells, this system will allow the generation of OA models with specific etiology/pathology/genetic backgrounds, as well as the simultaneous testing of tissue health as a whole. The outcomes gathered from studying the OA microJoint will be based on the use of the whole “joint”, representing human, not animal tissue, and incorporate multiple disease initiators. This system is also capable of simulating the patient-specific etiology of OA and predicting drug sensitivity, thus representing a robust tool to inform clinical trial design and implementation.

Acknowledgements

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